Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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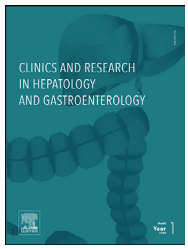

LETTER TO THE EDITOR

Liver injury after mRNA-based SARS-CoV-2 vaccination in a liver transplant recipient

KEYWORDS
Covid-19;
Vaccine;
Liver transplantation;
Toxicity

Coronavirus disease-2019 (Covid-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is an ongoing global pandemic of major concern, started at the end of 2019. Patients with comorbidities are at high risk of developing severe disease and this includes solid organ transplant recipients [1]. Therefore, Covid-19 vaccine is highly recommended in this population. Neverthless, immunocompromised patients, including solid organ transplant recipients, were not included in the Covid-19 vaccine large trials, especially of Pfizer/BioNTech and Moderna mRNA vaccines, and therefore, safety and efficacy data are lacking in this population. Recently, a significantly reduced immunogenicity of the mRNA SARS-CoV-2 vaccines has been reported [2,3]. Regarding the massive number of patients receiving this vaccination, identification of clinically relevant imputable side-effects of the vaccines is very difficult and therefore a major goal.

Herein we report the case of a 46-year-old male, who received the first injection of BNT162b2 mRNA vaccine 123 days after a liver transplantation for alcohol-associated liver disease. At the time of vaccination, the patient was on maintenance immunosuppression therapy with tacrolimus and mycophenolate mofetil, and liver function tests were within normal range. According to systematic biological follow-up, 12 days after vaccination, laboratory findings were as follows: AST 99 U/l (normal: 10—45), ALT 287 U/l (normal: 10—45), alkaline phosphatase (ALP) 270 U/l (normal: 38—120), gamma glutamyl transferase (GGT) 797 U/l (normal: 7—65), total bilirubin 9 mmol/l (normal: 0—20). The patient was totally asymptomatic. Serum HBsAg, anti-HBs, anti-HBc IgM, anti-HAV IgM, anti-HEV IgM, EBV-DNA (PCR), CMV-DNA (PCR), antinuclear antibody, anti-smooth muscle antibody, and anti-liver kidney microsomal antibody were negative. The patient did not consume alcohol on a regular or irregular basis. Other than immunosuppressive treatments included only aspirin. Abdominal Doppler ultrasound was normal. The diagnosis of liver damage related to vaccination was considered and no further investigation was performed, including no liver biopsy. Similarly, no modification of immunosuppressive regimen was done. The second vaccine injection was contra-indicated. Biological evolution was rapidly favourable. One month after initial biological liver injury, laboratory findings were as follows: AST 19 U/l (normal: 10—45), ALT 24 U/l (normal: 10—45), ALP 117 U/l (normal: 38—120), GGT 101 U/l (normal: 7—65), total bilirubin 8 mmol/l (normal: 0—20).

We report herein the case of a liver transplant recipient who presented mild liver injury probably due to the first injection of BNT162b2 mRNA vaccine. Evolution was spontaneously favourable. Perturbation of liver function tests was transitory, but detected because of regular systematic (monthly) biological follow-up, less than one year after transplantation. In this context, such diagnosis must be considered together with more usual cause of liver graft injury, such as rejection, in face of significant liver function test abnormalities. Moreover, in the absence of severe liver injury, deleterious manoeuvres (diagnostic or therapeutic) must be ovoid and close biological follow-up performed. The most intuitive expected toxicity of mRNA vaccine (but also all vaccines) is related to immune activation. Therefore, benign and common reported symptoms include soreness, fatigue, myalgia, headache, chills, fever, joint pain, nausea, muscle spasm, sweating, dizziness, flushing, feelings of relief, brain fogging, anorexia, localized swelling, decreased sleep quality, itching, tingling, diarrhoea, nasal stuffiness and palpitations [4]. The flip side of the possibly beneficial adjuvant inflammation, however, is potential toxicity of the mRNA vaccines. And remember that this type of vaccine has also been evaluated as an anti-cancer treatment. With the Covid-19 vaccines, we are using this new type of vaccine for the first time on a very large scale. From preliminary animal and human studies on previous mRNA vaccines, the clinical adverse effects have included myopathy (caused by mitochondrial toxicity), lipodystrophy, lactic acidosis, pancreatitis, liver steatosis, and nerve damage and some were severe [5]. A better understanding of the toxicity of Covid-19 vaccines, particularly mRNA vaccines, can only be based on comprehensive reporting of even apparently mild cases.

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These cases will be more easily identified in special populations under close clinical and biological surveillance, such as transplant patients, as reported in our patient. Perhaps these patients are also at greater risk.

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